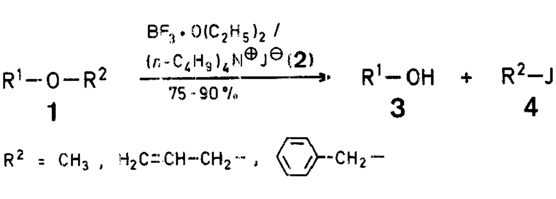
Boron Trifluoride Etherate/Iodide Ion as a Mild, Convenient and Regioselective Ether Cleaving Reagent

Arun K. Mandal*, N. K. Soni, K. R. Ratnam

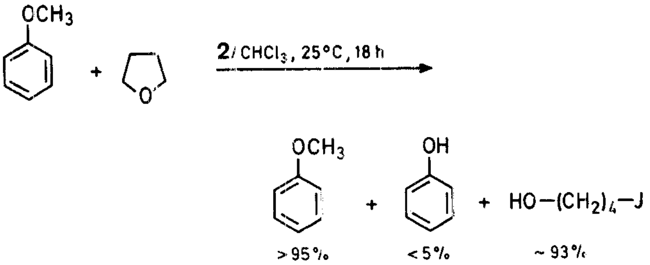
Alchemie Research Centre Private Limited, CAFI Site, P.O. Box 155, Thane-Belapur Road, Thane 400601, Maharashtra, India

The cleavage of ethers is an important and versatile reaction in organic synthesis. Many reagents are capable of cleaving ethers as discussed in several earlier reviews[1]. Especially the recently published exhaustive review[2] describes a number of boron containing reagents, namely, boron trichloride, boron tribromide and boron triiodide as excellent reagents for the cleavage of aromatic and aliphatic ethers. These boron reagents are mild and powerful ether cleaving agents and do not, therefore, differentiate between aliphatic and aromatic ethers. Few reports, however, exist on the use of boron trifluoride as an ether cleaving agent, although a combination of boron trifluoride etherate and ethanedithiol[2] is reported to cleave only benzyl ethers.

We now report that a combination of boron trifluoride etherate/tetrabutylammonium iodide (reagent **2**) in chloroform or dichloromethane, is a mild, inexpensive and highly selective reagent for the cleavage of aliphatic ethers **1** to the corresponding alcohols **3** in high yields. It is also possible to replace tetrabutylammonium iodide by potessium iodide as a source of iodide ion. Thus, alkyl ethers such as 1-octyl methyl ether, 2-octyl-methyl ether are cleaved to yield the corresponding octanols. Functionally substituted ether such as allyl octyl ether is cleaved cleanly to 1-octanol. Cyclic ether such as tetrahydrofuran is cleaved smoothly to 4-iodobutanol (Table).



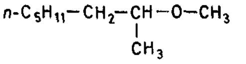
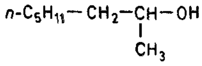
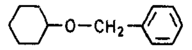
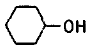
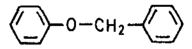
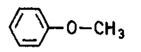
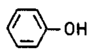
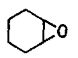
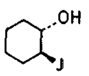
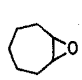
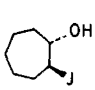
Aromatic ethers react extremely sluggishly with the reagent **2** under the reaction condition used (entry 7, Table). This permitted a selective cleavage of an aliphatic ether over an aromatic ether.



Phenyl benzyl ether is totally inert to the reagent **2** even under drastic condition (entry 6, Table). This result is in contrast to the reagent boron trifluoride etherate/ethanedithiol[2] which cleavaes benzyl ether cleanly. Cyclohexyl benzyl ether, however, is cleaved by **2** to cyclohexanol and benzyl iodide (entry 5, Table).

The reagent **2** also cleaves epoxides to *trans*-2-iodoalkanols. Thus, cyclohexene and cycloheptene epoxides are cleaved to the corresponding *trans*-2-iodocycloalkanols (entries 8 and

Table. Cleavage of Ethers **1** to Alcohols **3** with Reagent **2**

Entry	Substrate **1**	Product **3**[a]	Solvent	Reaction Conditions Time/Temp.	Yield[b] [%]	b.p. [°C]/torr or m.p. [°C] found	b.p. [°C]/torr or m.p. [°C] reported
1	$n\text{-}C_7H_{15}-CH_2-O-CH_3$	$n\text{-}C_7H_{15}-CH_2-OH$	$CHCl_3$	3 h/65 °C	85	105–106°/30	98°/19[3]
2	$n\text{-}C_7H_{15}-CH_2-O-CH_2-CH=CH_2$	$n\text{-}C_7H_{15}-CH_2-OH$	$CHCl_3$	5 h/65 °C	75		
3	 $n\text{-}C_5H_{11}-CH_2-\underset{\mid \atop CH_3}{CH}-O-CH_3$	 $n\text{-}C_5H_{11}-CH_2-\underset{\mid \atop CH_3}{CH}-OH$	$CHCl_3$	3 h/65 °C	86 (95)	92–93°/30	84°/15[3]
4		$J-(CH_2)_3-CH_2-OH$	$CHCl_3$ THF[c]	3 h/65 °C 12 h/25 °C	90 85	104°	104.5°[4]
5			$CHCl_3$	3 h/65 °C	80	160°/760	161°/760[5]
6		–	$CHCl_3$	12 h/65 °C	no reaction		
7			$CHCl_3$ $CHCl_3$	6 h/65 °C 14 h/25 °C	(20) (7)		
8			CH_2Cl_2	4 h/25 °C	70 (93)	38–40°	39–40.5°[6]
9			CH_2Cl_2	4 h/25 °C	72 (93)	–[e]	$C_7H_{13}IO$ (240.1)[f]

[a] All products displayed appropriate I. R. and ^{1}H-N. M. R. spectra and gave single spot on T. L. C. analysis. The liquid products are >95% pure by G. L. C. analysis; column: 3% OV17 on Celite 100/200 mesh (5′ × 0.25″).

[b] Yield of isolated product, value in brackets is yield by G. L. C.

[c] Boron trifluoride etherate/potassium iodide was used as the cleaving reagent.

[d] The stereochemistry is assigned based on *trans*-2-iodocyclohexanol; purity 99% according to G. L. C.
I. R. (Film): $\nu = 3490\ cm^{-1}$ (OH).
^{1}H-N. M. R. (CDCl$_3$/TMS): $\delta = 1.30$–1.70 (m, 6H, CH$_2$); 1.80–2.50 (m, 5H, C$\underline{H}_2$—CH—O$\underline{H}$, C$\underline{H}_2$—CH—J); 3.60–4.40 (m, 2H, C$\underline{H}$—OH, C$\underline{H}$—J).
M. S.: $m/e = 240$ (M$^+$).

[e] Distillation under vacuum is accompanied by decomposition.

[f] calc. C 35.00 H 5.42 O 6.67
found 35.19 5.30 6.34

9, Table). In both cases the corresponding rearranged cycloalkanone is formed in 5–6% yield. We are currently exploring the scope of this new reagent for other useful synthetic transformations.

Cleavage of Ethers with 2; General Procedure:

To a stirred solution of ether **1** (20 mmol) and *n*-tetrabutylammonium iodide (6.74 g, 21 mmol) in dry chloroform (25 ml) is added through a syringe boron trifluoride etherate (2.4 g, 21 mmol) and the mixture is stirred at room temperature or under reflux (Table). The mixture is then treated with saturated sodium hydrogen carbonate solution (25 ml) and extracted with chloroform (2 × 25 ml). The organic layer is washed with aqueous sodium thiosulfate solution (20 ml) followed by water (50 ml), dried with anhydrous sodium sulfate, and evaporated. The residue is then taken in ether (25 ml) and triturated. The ether layer is decanted from the precipitated salt; and distilled to yield the pure alcohol.

Cleavage of Cyclohexene Oxide with 2; Typical Procedure:

To a stirred solution of feshly distilled cyclohexene oxide (1.96 g, 20 mmol) and *n*-tetrabutylammonium iodide (7.7 g, 24 mmol) in dry dichloromethane (25 ml) is added dropwise through a syringe freshly distilled boron trifluoride etherate (2.7 g, 24 mmol) and the mixture is stirred at room temperature for 4 h. Hydrolysis of an aliquot followed by G. L. C. analysis reveals ~ 6% of cyclohexanone and 93% of *trans*-2-iodocyclohexanol. The mixture is then treated with saturated sodium hydrogen carbonate solution (25 ml) and extracted with dichloromethane (2 × 25 ml). The organic layer is washed with aqueous sodium thiosulfate solution (20 ml) followed by water (50 ml), dried with anhydrous sodium sulfate and evaporated. The residue is then treated with ether (25 ml) and cooled to precipitate the salt. The ether layer is decanted and the solvent removed to yield 4.0 g of the crude residue. The residue is purified by column chromatography over neutral alumina using *n*-hexane as eluent to give pure *trans*-2-iodocyclohexanol as a colourless liquid which solidifies in the refrigerator; yield: 3.14 g (70%); p. 38–40 °C (Lit.[6], m.p. 39–40.5 °C).

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* Address for correspondence.

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